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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ROSARIO LIZIO, HANS-ULRICH PETEREIT, ERNA ROTH, INES ANDRES, and MICHAEL DAMM

Appeal 2010-008567
Application 10/564,096
Technology Center 1600

Before DONALD E. ADAMS, DEMETRA J. MILLS, and ERIC GRIMES, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This appeal under 35 U.S.C. § 134 involves claims 1, 3, 4, 6-11, and 33-35 (App. Br. 2).[2] We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF THE CASE

The claims are directed to an oral multiparticulate pharmaceutical form (claims 1, 3, 4, 6-11, and 33) and a composition containing pellets

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[1] Oral Hearing held October 20, 2011.
[2] "Claims 2, 5 and 12-32 have been withdrawn from consideration by the Examiner" (App. Br. 2).

ranging in size from 50 to 2,500 μm (claims 34 and 35). Claims 1, 33, and 34 are representative and are reproduced in the "Claims Appendix" of Appellants' Brief (App. Br. 27 and 36).

Claims 33 and 34 stand rejected under the written description provision of 35 U.S.C. § 112, first paragraph.

Claim 34 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Shimono.[3]

Claims 1, 3, 6-11, and 34 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Watts.[4]

Claims 1, 3, 4, 6-11, and 34 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Watts and Berliner.[5]

Claims 1, 3, 4, 6-11, and 34 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Watts and Engel.[6]

Claims 1, 4, 33, and 34 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Shimono and Watts.

Claims 1, 4, 9, 10, and 33-35 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Shimono, Watts, and Engel.

We reverse the rejections under 35 U.S.C. § 112, first paragraph and affirm the prior art rejections.

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[3] Shimono, et al., EP 1 203 590 A1, published May 8, 2002.
[4] Watts et al., US 6,465,626 B1, issued October 15, 2002.
[5] Berliner et al., US 5,849,327, issued December 15, 1998.
[6] Engel et al., US 5,773,032, issued June 30, 1998.

Written Description:

ISSUE

Does the preponderance of evidence on this record support the Examiner's conclusion that Appellants' Specification fails to provide written descriptive support for the claimed invention?

Claim 33:

FACTUAL FINDINGS (FF)

FF 1. The Examiner finds that "[t]he only mention of 'gelatin' in . . . [Appellants'] [S]pecification is that the pellets of the pharmaceutical formulation can be placed in a gelatin capsule" (Ans. 12; *see* Spec. 33: 20-21; *see also* Reply Br. 14 ("Admittedly, the Specification does not expressly describe a composition that 'does not contain gelatin' in its inner matrix layer in those precise words"); App. Br. 23).

FF 2. Appellants exemplify a number of oral multiparticulate pharmaceutical formulations comprising an inner matrix that does not contain gelatin (*see* Spec. 51-52: Table 8).

ANALYSIS

Because Appellants' Specification does not expressly state that the inner matrix layer does not include gelatin, the Examiner finds that the language of claim 33 "excluding gelatin from the inner matrix layer" is new matter to Appellants' Specification (Ans. 11-12; FF 1). We are not persuaded. As Appellants explain "[*i*]*psis verbis* or a literal description of a claimed composition is not required in the Specification if it was clear that the Appellants had possession of the invention" (App. Br. 23). In this regard, Appellants contend that their "Specification provides a wealth of

examples of pellets wherein the inner matrix does not contain gelatin" (*id.*). We agree (*see* FF 2).

CONCLUSION OF LAW

The preponderance of evidence on this record fails to support the Examiner's conclusion that Appellants' Specification fails to provide written descriptive support for the claimed invention. The rejection of claim 33 under the written description provision of 35 U.S.C. § 112, first paragraph is reversed.

Claim 34:

FACTUAL FINDINGS (FF)

FF 3. The Examiner finds that Appellants' Specification fails to describe "'a mucoadhesive lipophilic matrix embedded in the inner matrix'" (Ans. 11).

FF 4. Appellants' Specification describes the lipophilic matrix as part of the inner matrix layer (Spec. 43: 9-12).

FF 5. Appellants' Specification discloses that "[t]he lipophilic matrix may consist of a single substance, e.g., of a lipid, or of a mixture of substances, e.g., of a mixture of lipids" (Spec. 35: 7-9).

FF 6. Appellants' Specification describes "[l]ipophilic matrix/polymers having a mucoadhesive effect" (Spec. 37: 35 (emphasis removed); *see also* Spec. 37: 36 - 38: 12).

ANALYSIS

The Examiner finds that because the term "mucoadhesive lipophilic matrix" is not expressly disclosed in Appellants' Specification "the ingredient cannot be excluded from the compositions as claimed" (Ans. 11;

see FF 3). We are not persuaded. As Appellants explain, their Specification discloses (1) that the lipophilic matrix is a component of the inner matrix and (2) "[l]ipophilic matrix/polymers having a mucoadhesive effect" (App. Br. 22-23 (emphasis removed); FF 4 and 6). Appellants' Specification also discloses that the lipophilic matrix may consist of a single substance, such as a lipid (FF 5). Therefore, having described a lipophilic matrix that has a mucoadhesive effect and a liphophilic matrix comprised of a single substance, such as a lipid, Appellants have descriptive support for a composition that does not have a mucoadhesive lipophilic matrix embedded in the inner matrix as claimed.

CONCLUSION OF LAW

The preponderance of evidence on this record fails to support the Examiner's conclusion that Appellants' Specification fails to provide written descriptive support for the claimed invention. The rejection of claim 34 under the written description provision of 35 U.S.C. § 112, first paragraph is reversed.

Anticipation:

ISSUE

Does the preponderance of evidence on this record support the Examiner's finding that Shimono teaches the claimed invention?

FACTUAL FINDINGS (FF)

FF 7. Shimono teaches a composition comprising a Nonpareil® 103 pellet, coated with the active pharmaceutical ingredient, acetaminophen, to provide a medicament-containing core (Shimono 7, col. 12, ll. 44-49).

FF 8. Shimono's medicament-containing cores are coated with Eudragit® RS to provide a chitosan-dispersing Eudragit® RS-coated preparation (Shimono 7, col. 12, ll. 49-54).

FF 9. Shimono's chitosan-dispersing Eudragit® RS-coated preparation is then coated with Eudragit® L100-55 to produce a colonic delivery pellet preparation (Shimono 8, col. 13, ll. 1-8).

FF 10. Appellants' Specification discloses that chitosan is a polymer having a mucoadhesive effect (Spec. 12: 11-12).

ANALYSIS

> The Examiner finds that
>
> > Together the non-pareil, chitosan, active ingredient and EUDRAGIT® RS form the inner matrix of the composition and there is no layer separating those ingredients from the outer coating of EUDRAGIT® L. No ingredient identified as a mucoadhesive lipophilic matrix is present in the inner matrix. The outermost coating is an enteric polymer that meets the pH limitations of claim 34.

(Ans. 8.) We find no error in the Examiner's findings or reasoning.

Appellants contend that Shimono fails to teach a "medicament-containing material . . . combined with chitosan in an inner matrix as in Applicant's [sic] Claim 34" (App. Br. 17; Reply Br. 9). In this regard, Appellants contend that "Shimono's core appears to be separated from the chitosan in the inner matric [sic] by the water-insoluble polymer" (*id.*; Reply Br. 10). We are not persuaded. Appellants' claim 34 does not exclude an inner matrix composed of separate layers of active pharmaceutical ingredient and polymer.

There is no persuasive argument or evidence to support Appellants' contention that the chitosan present in the composition of claim 34 exhibits

different properties than the chitosan in Shimono's composition (App. Br. 17-18; Reply Br. 10-11). There is also no persuasive argument or evidence to support Appellants' contention that the composition of claim 34 exhibits a different dissolution profile than Shimono's composition (App. Br. 19; Reply Br. 11). Argument by counsel cannot take the place of evidence. *In re Geisler*, 116 F.3d 1465, 1471 (Fed. Cir. 1997).

For the reasons set forth above Shimono's composition appears to be identical to the composition of Appellants' claim 34. "[W]hen the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990). Appellants failed to carry their burden.

CONCLUSION OF LAW

The preponderance of evidence on this record supports the Examiner's finding that Shimono teaches the claimed invention. The rejection of claim 34 under 35 U.S.C. § 102(b) as being anticipated by Shimono is affirmed.

Obviousness:

Watts alone:

ISSUE

Does the preponderance of evidence on this record support a conclusion of obviousness?

FACTUAL FINDINGS (FF)

FF 11. Watts suggests "a composition comprising a mixture of chitosan and type A cationic, gelatin, together with a therapeutic agent" (Watts, col. 3, ll. 7-10; Ans. 3).

FF 12. "The term 'type A gelatin' includes all cationic proteins which are, or may be, obtained by partial acid hydrolysis of animal collagen, and excludes type B gelatins" (Watts, col. 3, ll. 58-60).

FF 13. Watts suggests compositions "in the form of microparticles" (Watts, col. 3, ll. 61-65; Ans. 3).

FF 14. Watts suggests compositions coated with enteric polymers, such as EUDRAGIT®, for delivery of the therapeutic agent to the small intestine or colon (Watts, col. 7, ll. 10-25; Ans. 4).

FF 15. The Examiner finds that EUDRAGIT® polymers dissolve in a "pH from 4.0 to 8.0" (Ans. 4).

FF 16. The Examiner finds that chitosan is a mucoadhesive polymer that has a mucoadhesive effect within the parameters required by Appellants' claimed invention (Ans. 5).

FF 17. Watts suggests that

> when the compositions according to the invention are provided in the form of microparticles, such microparticles retain a positive charge and may provide for the improved transport of polar drugs across, or for the improved presentation of vaccines to mucosal surfaces, such as the nasal cavity, to such an extent that the effect is superior to that obtained from a chitosan solution, or microparticles produced from chitosan or type A gelatin alone.

(Watts, col. 4, ll. 1-9.)

FF 18. Watts suggests that "[t]he compositions may gel on the mucosa at least to some extent and this may facilitate retention of the composition on the mucosa" (Watts, col. 7, ll. 2-4).

ANALYSIS

We find no error in the findings, analysis and conclusion of obviousness as set forth by the Examiner (Ans. 3-6). Appellants contend that Shaheen[7] supports a conclusion that "[g]elatin is a bioadhesive polymer" (App. Br. 13). Accordingly, Appellants contend that Watts' composition comprising 50% gelatin and 50% chitosan "is not a mucoadhesive polymer" and "does not comprise a polymer having a mucoadhesive effect" (*id.* at 12). We are not persuaded.

Appellants fail to establish an evidentiary basis to support a conclusion that Watts' type A gelatin is the same as, and/or would have been expected to exhibit the same properties as, Shaheen's gelatin (*see* FF 11 and 12). In addition, Appellants fail to establish that chitosan would fail to exhibit its intrinsic properties when mixed in equivalent proportions with type A gelatin. The evidence of record fails to support Appellants' contention that Watts' 50:50 mixture of type A gelatin and chitosan "is retained by, the mucosal surface to an extent superior to either gelatin or chitosan alone (Watts, col. 4, ll. 1-10)" (App. Br. 13; *Cf.* FF 17). While the portion of Watts relied upon by Appellants suggests that the combination of type A gelatin and chitosan provides for the improved transport of polar drugs across mucosal surfaces or the improved presentation of vaccines to

[7] Sharif Mohammad Shaheen et al., *Effect of Bio-adhesive Polymers like HPMC, Gelatin, Na-CMC and Xanthan Gum on Theophylline Release from Respective Tablets*, 2(5) INTL. J. PHARMACOL. 504-508 (2006).

mucosal surfaces, it does not suggest that the composition is retained by the mucosal surface (FF 17). Further, while Watts suggests that compositions within the scope of Watts' invention "*may* gel on the mucosa at least to some extent," we find no persuasive evidence or argument on this record to support a conclusion that Watts' composition comprising a 50:50 mixture of type A gelatin and chitosan *does* gel on the mucosa or, even if it does, that the chitosan in such a mixture would fail to exhibit its mucoadhesive effect (FF 18 (emphasis added)).

For the reasons set forth above, we are not persuaded by Appellants' contentions regarding claims 1 and 34 (App. Br. 14).

CONCLUSION OF LAW

The preponderance of evidence on this record supports a conclusion of obviousness. The rejection of claims 1 and 34 under 35 U.S.C. § 103(a) as unpatentable over Watts is affirmed. Because they are not separately argued, claims 3 and 6-11 fall together with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

The combination of Watts and Berliner:

ISSUE

Does the preponderance of evidence on this record support a conclusion of obviousness?

FACTUAL FINDINGS (FF)

FF 19. The Examiner relies on Watts as discussed above (Ans. 6).

FF 20. The Examiner relies on Berliner to suggest that "coating thickness may vary but in general, coating thicknesses of about 0.1 to about 1.0 mm (100 μm - 1,000 μm) provide the best results" (*id.*).

ANALYSIS

Based on the combination of Watts and Berliner, the Examiner concludes that "[i]t would have been obvious to one of ordinary skill in the art to apply an enteric coating of the thickness of 100 μm - 1,000 μm . . . to the compositions taught by Watts" (*id.*). We find no error in the Examiner's prima facie case of obviousness.

Appellants contend that Berliner fails to make up for the deficiencies in Watts (App. Br. 15). Having found no deficiencies in the Examiner's reliance on Watts, we are not persuaded.

CONCLUSION OF LAW

The preponderance of evidence on this record supports a conclusion of obviousness. The rejection of claim 1 under 35 U.S.C. § 103(a) as unpatentable over the combination of Watts and Berliner is affirmed. Claims 3, 4, 6-11, and 34 fall together with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

The combination of Watts and Engel:

ISSUE

Does the preponderance of evidence on this record support a conclusion of obviousness?

FACTUAL FINDINGS (FF)

FF 21. The Examiner relies on Watts as discussed above (Ans. 7).

FF 22. The Examiner relies on Engel to suggest cetrorelix as a suitable therapeutic agent for inclusion in Watts' composition (*id.*).

ANALYSIS

Based on the combination of Watts and Engel, the Examiner concludes that, at the time of Appellants' invention, it would have been prima facie obvious to a person of ordinary skill in the art to utilize cetrorelix as the therapeutic agent in Watts' composition (*id.*).

Appellants contend that Engel fails to make up for the deficiencies in Watts (App. Br. 15). Having found no deficiencies in the Examiner's reliance on Watts, we are not persuaded.

CONCLUSION OF LAW

The preponderance of evidence on this record supports a conclusion of obviousness. The rejection of claim 1 under 35 U.S.C. § 103(a) as unpatentable over the combination of Watts and Engel is affirmed. Claims 3, 4, 6-11, and 34 fall together with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

The combination of Shimono and Watts:

ISSUE

Does the preponderance of evidence on this record support a conclusion of obviousness?

FACTUAL FINDINGS (FF)

FF 23. The Examiner relies on Shimono and Watts as discussed above (Ans. 9).

ANALYSIS

Based on the combination of Shimono and Watts the Examiner concludes that Shimono "demonstrates that microcapsules . . . need not be constructed with an inner matrix containing gelatin and can be made using

chitosan without gelatin" (Ans. 10). Watts suggests the use of EUDRAGIT® polymers as enteric coatings (FF 14). Accordingly, we find no error in the Examiner's conclusion that it would have been prima facie obvious to a person of ordinary skill in this art to utilize Shimono's EUDRAGIT® L as the enteric coating of Watts' composition (Ans. 9-10). Therefore, we are not persuaded by Appellants' contention that the Examiner fails to establish a nexus between the compositions of Shimono and Watts that "would have led persons having ordinary skill in the art to reasonably believe that any elements of Shimono's delivery compositions might or should be replaced by any elements of Watts' delivery compositions and vice versa" (App. Br. 20).

For the reasons set forth above, we are not persuaded by Appellants' contention that "[t]he Office has not provided any evidence that either Watts' mixture of gelatin and chitosan or Shimono's mixture of a water-insoluble polymer and chitosan is a mucoadhesive polymer or comprises a polymer having, exhibiting, or providing a mucoadhesive effect in the composition which defines the inner matrix" (*id.*; *see also* Reply Br. 11-13). Instead, for the reasons set forth above, we find that Shimono alone anticipates Appellants' claim 34 and that, at the time of Appellants' claimed invention, a person of ordinary skill in this art would have recognized that Appellants' claim 1 is prima facie obvious over Watts alone.

CONCLUSION OF LAW

The preponderance of evidence on this record supports a conclusion of obviousness. The rejection of claim 1 under 35 U.S.C. § 103(a) as unpatentable over Shimono and Watts is affirmed. Since they are not

separately argued, claims 4, 33, and 34 fall together with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

The combination of Shimono, Watts, and Engel:

ISSUE

Does the preponderance of evidence on this record support a conclusion of obviousness?

FACTUAL FINDINGS (FF)

FF 24. The Examiner relies on Shimono, Watts, and Engel as discussed above (Ans. 10).

FF 25. The Examiner finds that Engel "teaches that cetrorelix is a LHRH analog and is therefore functionally equivalent to the LHRH analogs taught by Watts" (*id*. at 10-11).

ANALYSIS

Based on the combination of Shimono, Watts, and Engel the Examiner concludes that, at the time of Appellants' invention, it would have been prima facie obvious to a person of ordinary skill in the art to utilize cetrorelix as the therapeutic agent in the compositions suggested by Shimono and Watts (Ans. 10-11).

Appellants contend that "[t]he problem with the Examiner's rationale is that no combination of Shimono and Watts would have led to the delivery compositions [of] Applicant[s'] claim[1]" (App. Br. 22). We are not persuaded for the reasons set forth above. Appellants further contend that "without some guidance, teaching, incentive, or motivation to combine cetrorelix with a mucoadhesive polymer having a mucoadhesive effect, persons having ordinary skill in the art would have had no reason to make

and use Applicant's [sic] claimed multiparticulate pharmaceutical form with any reasonable expectation of success" (*id.*). We are not persuaded (*see* FF 25).

For the reasons set forth above, we find that Shimono alone anticipates Appellants' claim 34 and that, at the time of Appellants' claimed invention, a person of ordinary skill in this art would have recognized that Appellants' claim 1 is prima facie obvious over Watts alone.

CONCLUSION OF LAW

The preponderance of evidence on this record supports a conclusion of obviousness. The rejection of claim 1 under 35 U.S.C. § 103(a) as unpatentable over the combination of Shimono, Watts, and Engel is affirmed. Because they are not separately argued, claims 4, 9, 10, and 33-35 fall together with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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